

## **B. THE ABSTRACT**

The Examiner has indicated that the abstract contains more than 1 paragraph and exceeds 150 words. While Applicants disagree with the Examiner's position regarding the initially submitted Abstract, they have submitted herewith a substitute page containing a new, brief Abstract. No new matter has been added. It is respectfully submitted that the objection has now been rendered moot.

## **C. THE INVENTION**

In one aspect of the invention there are provided polymer conjugates which are useful as prodrugs in the treatment of various medical conditions. One of the advances provided by the claimed invention is the presence of terminal extension moieties which facilitate attachment of the biologically active parent compound to a linear or branched polymer. As pointed out in the paragraph bridging pages 5 and 6 of the specification, the extension groups provide significant advantages to the artisan. The prodrugs made according to the present invention have a more predictable degree of loading of the parent therapeutic molecule to the polymer carrier. Thus, the final products are substantially uniform polymeric conjugates which are easy to analyze and are highly reproducible. The rate of hydrolysis of the therapeutic compound from the polymer transport portion is also predictable and reproducible from batch to batch. A still further advantage is that in certain preferred embodiments, in which the polymer portion has a molecular weight of from about 20 to about 50 kDa, conjugates containing anti-tumor agents are believed to passively target tumors and thus enhance the effectiveness of the anti-tumor parent compound on solid tumors. While applicants are not bound by theory, it is believed that tumor proteases, alone and/or in combination with peptidases, cleave the covalent extender linkage between the polymer and active agent, thus freeing the parent active agent within the tumor.

#### D. DOUBLE PATENTING

In response to the provisional obviousness-type double patenting rejection, Applicants respectfully request that the Examiner reconsider and remove the rejection. The present invention is directed to polymer conjugates corresponding to Formula (I) and Formula (II). It is important to note that within these formulae, the variable G represents a linear or branched polymer residue and this polymer residue is attached to an extender-containing a linking group which facilitates attachment of the polymer residue to the B moiety, e.g. the residue of a hydroxyl- or amine-containing target or parent molecule. It is urged that a patentably distinct invention is claimed in commonly-assigned USSN 09/823,296. For example, while Formula (I) of the '296 application also includes a variable G which represents the same type of linear or branched polymer, it is not directly attached to the extender moiety. Specifically, in the case of the '296 application, the polymer G is attached to moieties which allow terminal branching of the polymer and thus allow much higher loading of the active material onto the polymer. The Examiner's attention is directed to the N-(E4)-J group of Formula (I) claimed in the '296 patent. It is this branching group which is attached to the extension group which corresponds to the extension group directly attached to G in the present invention. Thus, unlike the present invention where there is a direct attachment of the extension linking group to the polymeric G group, the '296 application requires that a different group, e.g. one which facilitates terminal branching, to be attached to the G group before the extender groups are attached. It is urged that it would not have been obvious to modify the present invention to provide that which is claimed in the '296 application or *vice versa*. While the '296 application and the present application were filed on the same day and share certain elements, it is urged that the claims of each are patentably distinct. Reconsideration and removal of the provisional rejection is therefore urged.

Applicants further argue in the alternative that if the provisional obviousness double patenting rejection is maintained, that the filing of the Terminal Disclaimer be delayed until a Notice of Allowability is received.

**E. REJECTION UNDER 35 U.S.C. §102(b)**

**Claims 1-15, 17-20 and 23-31 Are Not Anticipated By U.S. Patent No. 5,620,689**

At page 3 of the Office Action, the Examiner has rejected the subject matter of the above-mentioned claims under 35 U.S.C. §102(b), as being anticipated by U.S. Patent No. 5,620,689 (hereinafter the '689 patent). The Examiner has taken the position that Figs 2A-2B and Figs. 2A-4 of the '689 patent are viewed as being inclusive of Formula (I).

A rejection under 35 U.S.C. § 102(b) requires that all of the elements of the rejected claims be found within the cited reference. It is respectfully urged that all of the claimed elements are not described in the '689 patent and that the pending claims are not anticipated by the cited reference.

The '689 patent discloses liposomes which contain a surface coating of PEG chains. As shown in figure 1, some of the PEG chains are funtionalized for attachment to an antibody or antibody fragment. Before the antibody is attached, however, the other end of the PEG is attached to a lipid. This PEGylated lipid is used to form the liposome which, as pointed out in column 7 of the '689 patent beginning at line 28, entraps a therapeutically active compound. The PEG employed in the '689 patent has a molecular weight of only 500 to 10,000 daltons. In each and every aspect of the '689 patent, the PEG is a heterobifunctional derivative. As will be appreciated by the Examiner, the term "hetero" suggests that the functional group on each end of the PEG is different. For example, one functional group is designed to attach to the lipid while the opposite end of the polymer is functionalized with a different group such as a maleimide or similar group to facilitate attachment to the antibody. Unlike the present invention which employs either polymer residues which are capped on one end or homobifunctional polymers, the '689 patent must employ heterobifunctional terminal groups. If it did not, the artisan would end up with PEG strands having a lipid molecule attached on both ends thereof. There would be no possible place to attach the antibody since both reactive terminal groups would be linked to a lipid molecule.

The claimed invention, on the other hand is significantly distinguishable over the '689 patent. The claimed invention describes a polymer conjugate which contains the extender on one

end of the polymer residue (Formula (I)) or on both termini of a homobifunctional polymer derivative (Formula (II)) in which each end of the polymer (designated G in the formula) is substituted with the same extender group. Given these key differences in composition, it is further argued that the method claims - 25 and 26- and the method of treatment claims - 27 and 28- also distinguish over the '689 patent. There is absolutely no disclosure in the '689 patent which is sufficient to satisfy the burden of section 102(b) of 35 USC to render the claimed methods anticipated. It is respectfully urged that the Examiner reconsider and remove the rejection.

**F. INDICATION OF ALLOWABLE SUBJECT MATTER**

On page 5 of the Office Action, the Examiner has indicated that claims 16 and 22 would be allowable if re-written in independent form including all of the limitations of the base and intermediate claims. Applicants note with appreciation this indication but urge that all of the claims distinguish over the references of record.

**G. EXTENSION OF TIME PETITION**

This response is being filed with a petition for a two month extension of time and authorization to charge the fee therefor to deposit account 50-0217. No further fees are believed to be required. If, on the other hand, it is determined that any further fees are due or any overpayment has been made, the Assistant Commissioner is hereby authorized to debit or credit such sum to said deposit account.

Pursuant to 37 C.F.R. 1.136(a)(3), please treat this and any concurrent or future reply in this application that requires a petition for an extension of time for its timely submission as incorporating a petition for extension of time for the appropriate length of time. The fee associated therewith is to be charged to Deposit Account No. 50-0217.

**H. CONCLUSION**

In view of the actions taken and arguments presented, it is respectfully submitted that the present application is now in condition for allowance.

An early and favorable action on the merits is earnestly solicited.

Respectfully submitted,

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